

U.S. Patent Application Serial No. 10/069,977  
Response dated December 18, 2003  
Reply to OA of September 24, 2003

### **REMARKS**

Claims 4-9 and 12-16 are pending in this application. Amendments to claims 12 and 13 have been proposed herein.

#### **Regarding finality of the Office action.**

Applicants have respectfully petitioned under 37 CFR 1.181 on November 24, 2003, for withdrawal of the finality of the Office action of September 24, 2003. If the petition is granted and finality of that Office action is withdrawn, Applicants respectfully request that the present amendment be accordingly entered and considered.

**Claims 4, 5, 7-9 and 12-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hamad et al. (Journal of Applied Microbiology, 1997, Vol. 83, 764-770), in view of Wilding et al. (U.S. Pat. No. 5,498,392). (Office action paragraph no. 8)**

Reconsideration of the rejection is respectfully requested.

The Examiner cites Hamad's method of studying microflora of Sudanese sorghum flour as disclosing the elements of the claims except for the detector in which a probe is arranged on specific positions. Wilding is cited for the disclosure of such a detector.

In the Amendment of July 10, 2003, Applicants argued that the claims require "amplifying nucleic acid of an intestinal bacterial group ...", and that Hamad does not disclose or suggest this. This argument is relevant to all of claims 4, 5, 7-9 and 12-16. The Examiner responds to this argument on page 4, line 11, of the final Office action, by arguing that Hamad et al. discloses the study of *E. faecalis*, which the Examiner considers to be an intestinal bacterial flora.

In response, Applicants argue that “intestinal bacterial group” refers to the group of bacteria from an intestinal sample, not merely a bacterium which can be found in an intestine. The Examiner states on page 4, lines 15-20, that the disclosure of Hamad et al. would motivate one of skill in the art to analyze intestinal bacterial flora from a subject. The gist of the Examiner’s argument, however, appears to be that the motivation arises because it would be **possible** due to the similarity in the 16S rRNA. Applicants submit that this does not actually provide a **motivation** for the modification of the reference to have the “intestinal bacterial flora” limitation, but only an indication of reasonable expectation of success.

Applicants also argued in the Amendment that there is no teaching or suggestion in Hamad et al. or Wilding et al. for rapid simultaneous detection of a plurality of (strains of) bacteria, as is implied by the recitation of “intestinal bacterial group” in claim 5. The Examiner addresses these arguments on page 5, lines 5-14 of the final Office action. The Examiner states that Hamad et al. “was applied to detect a plurality of bacteria since the Sorghum flour contained more than one bacteria”, citing page 765, column 2, first and second paragraphs.

Applicants respectfully disagree with the Examiner’s reasoning. The fact that Hamad is studying different bacteria in the sorghum flour does not mean that Hamad is providing **rapid simultaneous detection** of these bacteria, and in particular Hamad et al. does not analyze based on the presence or absence of hybridization with a plurality of probes as recited in claim 5.

The Examiner cites Wilding et al. as disclosing a plurality of detection/reaction chambers to enable the rapid parallel detection of polynucleotides in a mixture, citing column 5, lines 9-11. In response, Applicants argue that even if Wilding’s device were capable of performing the method of claim 5, Wilding, too, fails to provide a motivation for analyzing an intestinal bacterial group as

U.S. Patent Application Serial No. 10/069,977  
Response dated December 18, 2003  
Reply to OA of September 24, 2003

recited in claim 5.

Moreover, even if Hamad et al. did suggest study of an intestinal bacterial group with a plurality of probes, this analysis could not be conducted in a single device of Wilding's. In the Wilding et al. device, there is no disclosure or suggestion of use of a plurality of probes, in particular where such probes are arranged on specific positions in a detector. It is not clear that the disclosure of Wilding et al. enables such a device.

Therefore, use of Wilding's devices for this purpose would require use of multiple devices, one for each probe. This, however, would be inconsistent with the recitation of claim 5, in which "said probes are arranged on specific positions on a detector."

Applicants therefore submit that claims 4, 5, 7-9 and 12-16 are novel and non-obvious over Hamad et al. and Wilding et al., taken separately or in combination.

**Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hamad et al. (Journal of Applied Microbiology, 1997, Vol. 83, 764-770) in view of Wilding et al. (U.S. Patent No 5,498,159) as applied to claims 4-5, 8-9 and 12-16, and further in view of Mullis et al. (U.S. Patent No. 4,800,159). (Office action paragraph no. 9)**

Reconsideration of the rejection is respectfully requested.

Applicants have argued above that the combination of Hamad et al. and Wilding et al. fails to provide the limitations of base claims 4 and 5.

Claim 6 requires that nucleic acid amplified from each intestinal bacterium (that is, each intestinal bacterium to be detected in the intestinal bacterial group) is used as a probe. Hamad et al. clearly does not disclose use of nucleic acid amplified from different bacteria for detection of those

U.S. Patent Application Serial No. 10/069,977  
Response dated December 18, 2003  
Reply to OA of September 24, 2003

bacteria.

The Examiner cites Mullis et al. as “[suggesting] that the intestinal bacterial flora would have been amplified and detected by hybridizing a nucleic acid probe. The amplified nucleic acid would have been used as probe because the amplified nucleic acid would have the same specificity as the probe used for the detection.”

Applicants, however, cannot find this suggestion (that a plurality of different probes, each obtained by amplification of a different intestinal bacterium, are used) in Mullis et al. and respectfully assert that Mullis et al. does **not** suggest this limitation of claim 6. The Examiner has not pointed out where in the reference this suggestion is made. Applicants submit that the Examiner’s general arguments regarding “same specificity” are directed to the “reasonable expectation of success”, but not to a suggestion or motivation for the claim limitation.

In the Amendment, Applicants argued that Mullis et al. relates to the detection of a single type of DNA fragment by amplification. The Examiner responds to this argument on page 8, fourth paragraph, of the final Office action, stating: “The reference of Mullis et al. provided is for the teaching of making the probe which is from the amplified nucleic acid.” Applicants do not dispute that one of skill in the art could make such a probe, but the making of the probe was not the issue in the rejection addressed in Applicants’ argument.

Applicants therefore submit that claim 6 is novel and non-obvious over Hamad et al., Wilding et al., and Mullis et al., taken separately or in combination.

**Claims 12-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant**

**regards as the invention.** (Office action paragraph no. 12)

a. The Examiner is correct that claims 12-16 depend improperly from canceled claim 11. Reconsideration of the rejection of point (a) is respectfully requested in view of the proposed amendment to claims 12 and 13. In the amendment, the claims are rewritten to incorporate the scope of canceled claim 11.

b. The Examiner states that claims 12-16 are “indefinite because the language ‘in which is arranged a probe’ in claim 12 is unclear as to whether the DNA chip has an immobilized probe arranged”. The Examiner appears to be questioning whether the term “arranged” means immobilized.

Reconsideration of this rejection is respectfully requested. Applicants assert that the term “arranged” in the claims refers to a probe immobilized on the DNA chip and that this meaning is clear from the specification. Applicants note, for example, that the specification on page 29, lines 14-24, discusses fabrication of DNA chips and uses the phrases “probe arrangement type” and “probe is arranged” on lines 17-18. Since DNA chips are well known in the art to have immobilized probes, Applicants submit that it can be clearly inferred that “arranged” here means “immobilized”. As such, the recitation of the claims is not indefinite.

The Examiner also states that in the phrase “having a nucleic acid sequence occurring” in claim 12, “it is unclear whether the nucleic acid sequence is comprised by the genome of the intestinal bacterial.” Applicants submit, however, that the phrase “having a nucleic acid sequence occurring in the genome” is clearly understandable.

The Examiner is requesting language using the word “comprising”, but this word is a transitional phrase word used to introduce the elements of a claim. The phrase “nucleic acid sequence

U.S. Patent Application Serial No. 10/069,977  
Response dated December 18, 2003  
Reply to OA of September 24, 2003

is **comprised by the genome**", suggested by the Examiner, would appear to be unclear. This would appear to be either defining the genome or stating that the nucleic acid includes the entire genome, neither of which is the intent of the claim.

The genome is a long DNA sequence, and the probe has a short DNA sequence which is a subsequence of the genome. Applicants submit that the present claim language can be clearly understood with reference to the present specification.

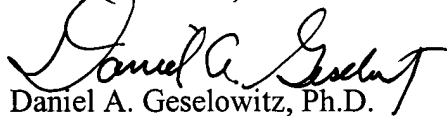
U.S. Patent Application Serial No. 10/069,977  
Response dated December 18, 2003  
Reply to OA of September 24, 2003

If, for any reason, it is felt that this application is not now in condition for allowance, the Examiner is requested to contact Applicant's undersigned agent at the telephone number indicated below to arrange for an interview to expedite the disposition of this case.

In the event that this paper is not timely filed, Applicant respectfully petitions for an appropriate extension of time. Please charge any fees for such an extension of time and any other fees which may be due with respect to this paper, to Deposit Account No. 01-2340.

Respectfully submitted,

ARMSTRONG, KRATZ, QUINTOS, HANSON & BROOKS, LLP



Daniel A. Geselowitz, Ph.D.

Agent for Applicant

Reg. No. 42,573

DAG/plb  
Atty. Docket No. 020159  
Suite 1000  
1725 K Street, N.W.  
Washington, D.C. 20006  
(202) 659-2930



23850

PATENT TRADEMARK OFFICE